UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,300	01/31/2007	Lynne Canne Bannen	EX04-018C-US	3595

63572 7590 09/22/2009

MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	
MAIL DATE	**DELIVERY MODE**
09/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,300	BANNEN ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *25,26,29,37,38,45-50 and 52-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,27,28,30-36,39-44 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 1-24, 27, 28, 30-36, 39-44 and 51, drawn to compounds and compositions where Ar = pyridine not further fused, in the reply filed on 6/26/2009 is acknowledged. Claims 1-24, 27, 28, 30-36, 39-44 and 51 will be examined to the extent they embrace the elected subject matter. Claims 25, 26, 29, 37, 38, 45-50 and 52-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter.

The traversal is on the ground that instant invention possesses unity of invention. This is not found persuasive.

First of all, as noted in the previous office action, there are two criteria for a proper requirement for restriction for a 371 of PCT application entering national stage.

Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Both these criteria are to be met with.

Contrary to applicants' urging, as noted above in the previous office action, instant inventions fail to meet both these conditions.

Applicants have argued that invoking In re Weber and In re Harnish that the restriction requirement is improper. Again this argument is not persuasive and the case laws cited are not the point. Careful analysis of the case laws will show that there is condition clause above set two criteria should be considered for establishing unity of

invention. To quote MPEP 803 'Since the decisions In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

As noted above, both these criteria have not been met with.

Applicants have not shown clearly or established what portion of the core share a substantial structural feature disclosed as being essential to that utility. Applicants assert that X-Ar-Y-L-Z share common utility and share structural feature essential for the utility. But applicants have not shown what this essential structural feature that contributes to the common utility. As recited , every X, Ar, Y, L and Z are variables and hence one can not arrive at a common structural feature. In addition, applicants have argued that the above said genus of compounds are Tie-2 inhibitors and therefore share common utility. This is incorrect. Inihibtion of Tie-2 is a mode of action not utility. The actual uses of these compounds are depicted in pages 69-71 of specification and uses include thousands of diseases. Hence, the common utility requirement is not met with. Even the International Search Authority has deemed instant invention as lacking unity of invention and has stated that " The claims relate to an extremely large number of permutations based on the scope of variables as genetically set forth in the claims

which are not all adequately supported in the description within the meaning of PCT Article 6. The claims have been searched based on representative examples set forth in claim 42.".

The fact that structurally related compounds of instant claims have different utility, which would negate the common utility requirement & sharing the substantial structural feature.

Examiner also noted in the previous office action "Should applicant traverse on the ground that the core species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention". Applicants have not asserted that the two groups are not distinct. Applicants have not submitted evidence or identified such evidence now of record showing the core group to be obvious variants or clearly admitted on the record that all core groups embraced in the instant inventions are equivalent. In which case, examiner needed not search all cores. A prior art which anticipates any one of the groups embraced by a specific core (i.e. choices of I or II) may then render rest of the core groups as obvious variant. In other words, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. It should be noted that applicants have excluded some prior art compounds by a proviso, which would be applicable to part of the genus as obvious

variant under 35 U.S.C. 103(a). In want of such assertion or evidence, unity of invention of the huge genus of compounds for proper examination is deemed as lacking as there is no equivalency and each group is distinct and independent.

It should be also noted that applicants have made only 281 compounds while genus encompasses over billion compounds and hence the genus cannot be considered as totally represented by the species. In fact the Internal Search Authority noted that in the reason for the limitation of the search:

"The claims relate to an extremely large number of permutations based on the scope of variables as genetically set forth in the claims which are not all adequately supported in the description within the meaning of PCT Article 6. The claims have been searched based on representative examples set forth in claim 42".

Hence, the instant claims fail to meet both the requirement stated above.

Based on the foregoing reasons, the requirement is still deemed proper and is therefore made FINAL.

It should be noted that although election of species is not a requirement in a PCT application entering national stage, as full scope of search is not possible with such a generic genus of over billion compounds, the current search is based on a genus of compounds encompassing the species elected by the applicants as guidance. More specifically prior art search in STN for the elected core resulted in incomplete search as the compounds exceeded 2 millions. The search was narrowed to a subgenus (4 times, See SRNTs in pair) of species elected.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed on 02/13/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24, 27, 28, 30-36, 39-44 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "prodrug" in claim 1, renders claim 1 and its dependent claims 2-24, 27, 28, 30-36, 39-44 and 51indefinite, as prodrug such as ester or carbamate in general and as noted in specification, are compounds, which undergo in vivo hydrolysis. In that sense recitation of "prodrug" is not ambiguous and is acceptable. However, the definition of various substituents groups on pyrimidine include such groups, namely esters, carbamates, alkoxycarbonyl etc. which are also in vivo hydrolysable and therefore it is not clear what is the difference between these variable groups and the "prodrug" groups. The use of ester group(s), carbamates etc as substituents as Markush choice, results in ambiguity. There is clear-cut ambiguity as to what is to be considered as prodrug and what is not. Applicants should note that if the variable groups are prodrug, which are in general inactive but becomes active upon in vivo transformation, then the compound bearing the variable group would be deemed as inactive which is not what the claim recites.

Furthermore, the issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' prodrugs are molecules whose structure lie outside the subject matter of formula (I), but upon metabolism in the body are converted to active compounds falling within the structural scope of formula (I). The claim describes the function intended but provides no specific structural guidance to what constitutes a “prodrug”. Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

2. Claims 44 and 51 are improper dependent claim as they recite a limitation “metabolite" which is not recited in claim 43 on which they are dependent. The independent claim 1 does not recite “metabolite” and hence the scope of claim 44 and 51 is outside the scope of claim 1. In addition, it is not clear what is the structural make-up of the “metabolite” is.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24, 27, 28, 30-36, 39-44 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry

- to use the invention. “The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims”, In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug , in this case in vivo hydrolysable ester is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism 'de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Thus, determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation. In addition, as it is not clear what the structural make-up of these metabolites is. The genus of compounds embraced in claim 1 would exceed, as is, trillion compounds. In addition, their derivatives and analogs etc. would quite likely to encompass the entire known chemical space. To find a prodrug in this space without any guidance is formidable task and hence claim 1 needs state the structural make-up of these prodrugs to search and examine. Specification has no showing or teaching of

any such prodrug. Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here. b) The direction concerning the prodrugs is found in the second paragraph of page 74 c) There is no working example of a prodrug of a compound the formula (I). d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modem Pharmaceutics) in the first sentence, third paragraph on page 596 states that “extensive development must be undertaken” to find a prodrug. I) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well established that “the scope of enablement varies inversely degree of unpredictability of the factors involved”, 'and physiological activity is generally considered to be an unpredictable factor. See In re

Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim I as well as the presently unknown list potential prodrug derivatives embraced by the word "prodrug". Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claims 1-24, 27, 28, 30-36, 39-44 and 51are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making pharmaceutically acceptable salts does not reasonably provide enablement for making hydrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence

or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to compound of formula I, or a pharmaceutically acceptable salt, hydrate …thereof. Specification is not adequately enabled as to how to make solvate of compounds of formula (I) Specification has no example of hydrate of the instant compounds. Specification recites solvate thereof but there is no enabling of such compounds.

The compound of formula I embrace pyridine compounds substituted with various variable groups. Even a cursory calculation of the number of compounds embraced in the instant formula (I) based on the generic definition of alkyl., aryl, heteroaryl, heterocyclyl, substituted aryl, heteroaryl, arylalkyloxy, arylalkylthio etc would result in trillions of compounds. This is of course not the accurate number and the true number of compounds would far exceed this number of compounds. Thus the genus embraced in the claim 1 is too large and there is no teaching of any hydrate of this large genus.

Search in the pertinent art, including water as solvent resulted in a pertinent reference, which is indicative of unpredictability of hydrate formation in general. The state of the art is that is not predictable whether solvates or hydrates will form or what their composition will be. In the language of the physical chemist, a hydrate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species

introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to hydrates, which means a different solvent or even the moisture of the air that might change the stabile region of the hydrate. In the instant case of hydrate a similar reasoning therefore applies. Water is a solvent and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to hydrate. Specification has no working example of solvate of compound of formula (I). See In re Howarth, 654 F.2d 103,210 USPQ 689 (CCPA 1981); Exparte Moersch, 104 USPQ 122 (POBA 1954). Specification is not adequately enabled as to how to make solvate of compounds of formula (I). Specification neither discloses what types of solvates are intended nor has any examples of solvates of the instant compounds. Specification recites hydrates but there is no enabling disclosure of such hydrates. The compound of formula I embrace substituted pyridine compounds substituted with various variable groups X, Y, L , Z R^1, R^2, R^3, R^4, R^5, R^6 etc. Careful calculation of the number of compounds embraced in the instant formula (I) shows a large number of compounds. Thus, the genus encompassed by the claims is excessively large and there is no teaching of any solvate of this large genus. Search in the pertinent art, including water

as solvent resulted in a pertinent reference, which is indicative of unpredictability of solvate formation in general.

In addition, an additional search resulted in Vippagunta et al., Advanced Drug Delivery Reviews 48: 3-26, 2001, which clearly states that formation of hydrates in unpredictable. See entire document especially page 18, right column section 3.4. Note Vippagunta et al., states “Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for series of related compounds”. This prediction would involve quantification of the myriad intermolecular forces within any proposed crystal structure as well as the ability to postulate the likely packing modes for a given molecule in all its configurations" (see page 11, col. 2).

Also, note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

2. The predictability or lack thereof in the art:

Hence, the hydrate as applied to the above-mentioned compounds claimed by the applicant are not art-recognized compounds and hence there should be adequate enabling disclosure in the specification with working example(s).

3. The amount of direction or guidance present:

Examples illustrated in the experimental section are limited to making the compounds not related to solvates or hydrates. There is no example of a solvate or hydrate of instant compound. Over 281 compounds were shown in the examples of the specification each of which has come in contact with water and other solvent but there is no showing that instant compounds formed solvates or hydrates. Hence it is clear that merely bring the compound with solvent or water does not result in solvate or hydrate and additional direction or guidance is needed to make them Specication has no such direction or guidance.

4. The presence or absence of working examples:

There is no working example of any solvate or hydrate formed. The claims are drawn to hydrate, yet the numerous examples presented all failed to produce a solvate or hydrate. These cannot be simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ...' no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates and hydrates of these compounds actually exists; if they did, they would have formed. Hence, there should be showing supporting that solvates and hydrates of these compounds exist and therefore can be made.

5. The breadth of the claims & the quantity of experimentation needed:

Specication has no support, as noted above, for compounds generically embraced in the claims 1-24, 27, 28, 30-36, 39-44 and 51 would lead to desired solvate, hydrate of the compound of formula I. As noted above, the genus embraces over million compounds and hence the breadth of the claim is broad. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired solvate of compound of formula I embraced in the instant claims in view of the pertinent reference teachings.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Heeres et al., US 5,811,426.

Heeres teaches several urea and thiourea derivative of piperazinyl-pyridine compounds of formula I for treating helicobacteria, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups X, Y, Z, R^1, R^2, R^3, R^4, R^5 and R^6. Note when A ring is pyridine ring, with the given definition of these variable groups, compounds taught by Heeres include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 9-10 for examples of various compounds, which include instant compounds.

Claims 1-10 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Heeres et al., US 5,728,700.

Heeres teaches several sulfonamide derivative of piperazinyl-pyridine compounds of formula I for treating helicobacteria, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups X, Y, Z, R^1, R^2, R^3, R^4, R^5 and R^6. Note when A ring is pyridine ring, with the given definition of these variable groups, compounds taught by Heeres include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 8-10 for examples of various compounds, which include instant compounds.

Claims 1-10 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Heeres et al., US 5,650,411.

Heeres teaches several Aryl-piperazinyl-pyridine compounds of formula I for treating helicobacteria, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups X, Y, Z, Ar, R^1, R^2, R^3, R^4, R^5 and R^6. Note when A ring is pyridine ring, with the given definition of these variable groups, compounds taught by Heeres include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 19-124 for examples of various compounds, which include instant compounds.

Claims 1-10 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Heeres et al., US 5,637,592.

Heeres teaches several acyl derivative of piperazinyl-pyridine compounds of formula I for treating helicobacteria, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups X, Y, Z, R^1, R^2, R^3, R^4, R^5 and R^6. Note when A ring is pyridine ring, with the given definition of these variable groups, compounds taught by Heeres include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 11-18 for examples of various compounds, which include instant compounds.

Claims 1-10 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Heeres et al., US 5,571,811.

Heeres teaches several sulfonamide derivative of piperazinyl-pyridine compounds of formula I for treating helicobacteria, which include instant compounds,

and composition. See column 1, formula I and note the definition of various variable groups X, Y, Z, R^1, R^2, R^3, R^4, R^5 and R^6. Note when A ring is pyridine ring, with the given definition of these variable groups, compounds taught by Heeres include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 8-11 for examples of various compounds, which include instant compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heeres et al., US 5,811,426, US 5,728,700, US 5,650,411, 5637,592 or 5,571,81.

Teachings of Heeres as discussed in the above 102 rejections are incorporated herein. As noted above, Heeres teaches several piperazinyl-pyridine compounds of formula I, which include instant compounds and composition.

Heeres differs in not exemplifying all piperazinyl-pyridine compounds generically embraced in compound of formula I. However, Heeres teaches equivalency of those compounds exemplified with those generically claimed. Hence, it would be obvious to one trained in the art to make the compounds of formula I including instant compounds using the teaching and guidance provided by the exemplified compounds and expect these compounds to have the use taught therein.

Claims 1-24, 27, 28, 30-36, 39-44 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linz et al., US 5,563,268.

Linz teaches several heterobiaryl compounds of formula I for treating helicobacteria, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups X_1, X_2, X_3,Y_1, Y_2, Y_3, Y_4 and E. Note when Y_1 and Y_2 is a bond, with the given definition of the other variable groups, compounds taught by Linz include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 25-39 for examples of various compounds.

Linz differs in not exemplifying piperazinyl or piperdinyl linked pyridine compounds generically embraced in compound of formula I. However, Heeres teaches equivalency of those compounds exemplified with those generically claimed. Hence, it would be obvious to one trained in the art to make the compounds of formula I including instant compounds using the teaching and guidance provided by the exemplified compounds and expect these compounds to have the use taught therein.

Claims 1-24, 27, 28, 30-36, 39-44 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pennell et al., US 7,449,576.

Pennell teaches several piperazine compounds of formula I for treating arthritis, which include instant compounds, and composition. See column 1, formula I and note the definition of various variable groups Ar^1, HAr, R^1 and L^1. Note when Ar^1 is pyridine substituted with R^2, with the given definition of all other variable groups, compounds taught by Pennell include instant compounds. See column 19, formula IVa. Again with the given definition of R^{2a}, R^{2b}, R^{2c} and R^{2d}, the compounds taught by Pennell include instant compounds. See figure 5C, 5I and 5J for pyridine linked piperazine compounds. See entire document for various preferred embodiments, process of making, composition and method of use. See column 31-132 for examples of various compounds made. See column 138-177 for structures of the compound tested. See compound 1062 and 1141 shown therein.

Pennell differs in not exemplifying piperazinyl-pyridine compounds wherein the pyridinyl ring is further substituted with 5 to 7-memmbered link with or without a linker generically embraced in compound of formula I. However, Pennell teaches equivalency of those compounds exemplified with those generically claimed. Hence, it would be obvious to one trained in the art to make the compounds of formula I including instant compounds using the teaching and guidance provided by the exemplified compounds and expect these compounds to have the use taught therein.

Claims 1-24, 27, 28, 30-36, 39-44 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braje et al., US 7,320,979.

Braje teaches several piperazine compounds of formula I for treating schizoprenia, which include instant compounds, and composition. See column 2, formula I and note the definition of various variable groups Ar, Q, R, R^1 and R^2. Note when Q is pyridine, with the given definition of all other variable groups, compounds taught by Braje include instant compounds. See entire document for various preferred embodiments, process of making, composition and method of use. Especially see column 9-34 for various species made. See column 46-62 for examples of various compounds made.

Braje differs in not exemplifying all piperazinyl-pyridine compounds generically embraced in compound of formula I. However, Braje teaches equivalency of those compounds exemplified with those generically claimed. Hence, it would be obvious to one trained in the art to make the compounds of formula I including instant compounds using the teaching and guidance provided by the exemplified compounds and expect these compounds to have the use taught therein.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any

inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624